TO ASSES THE PREDICTIVE VALUE OF CALCIUM CREATININE RATIO IN SPOT URINE SAMPLE FOR EARLY PREDICTION OF PRE ECLAMPSIA

DESSERTATION SUBMITTED IN FULFILMENT OF THE REGULATIONS FOR THE AWARD OF

MD OBSTETRICS AND GYNAECOLOGY

DIVISION OF OBSTETRICS AND GYNAECOLOGY

PSG INSTITUTE OF MEDICAL SCIENCES AND RESEARCH

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

GUINDY, CHENNAI, TAMILNADU, INDIA

APRIL 2014

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APRIL 2014

CERTIFICATE

CERTIFICATE

This is to certify that **Dr. SINDHU D** has prepared this dissertation entitled "To Asses the predictive value of calcium to creatinine ratio in spot urine sample for early prediction of pre eclampsia'' under my overall supervision and guidance in the Institute of PSG Institute of Medical Science and Research, Coimbatore in partial fulfillment of the regulations of Tamil Nadu **Dr. M.G.R Medical University** for the award of **M.D. Degree in Obstetrics and Gynaecology**.

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DECLARATION

DECLARATION

I hereby declare that dissertation entitled "To Asses the predictive value of calcium creatinine ratio in spot urine sample for early prediction of pre eclampsia" was prepared by me under the guidance and supervision of **Dr. KANCHANAMALAI MD DGO.,** PSG Hospitals Coimbatore.

The dissertation is submitted to the Dr. M.G.R. Medical University in partial fulfillment of the University regulations for the award of MD degree in Obstetrics and Gynaecology. This dissertation has not been submitted for the award of any Degree or Diploma.

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ACKNOWLEDGEMENT

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Dr. SINDHU D

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INTRODUCTION

INTRODUCTION

Hypertensive disorders during pregnancy constitute the most common medical disorders encountered by obstetricians. The incidence is 7% to 10 %, of which pre eclampsia and eclampsia constitute 70% and chronic hypertension 30%. It remains the leading cause for maternal mortality and morbidity worldwide accounting for 15 % to 20%.

Pre eclampsia/eclampsia is a multi organ disorder unique to human pregnancy. The typical renal lesionsis glomeruloendotheliosis, which is the swelling of the glomerular capillary endothelial and mesangial cells.

Involvement of renal system is well before the symptomatology of pre elampsia manifest.

Pritchard stated that the presence of chorionic villi in women with pre eclampsia causes vasospasm leading to development of hypertension and serious multiorgan dysfunction, specifically confined to placenta, kidneys, liver and sometimes brain.

As per many studies, presence of placenta is sufficient for development of pre eclampsia, there is no necessity of fetus, as pre eclampsia is seen is complete mole, there is no necessity of uterus as it can be seen in abdominal pregnancy also. So the pathogenesis of pre eclampsia will start as early as the trophoblastic invasion, so any insult at that time can lead to development of hypertension during pregnancy.

So prediction of pre eclampsia earlier helps in early intervention and prevention of pre eclampsia. So many research workers are more towards the way of predicting pre eclampsia there by, primary prevention.

According to World Health Organization, hypertensive diseases during pregnancy are a major cause of perinatal mortality and morbidity. Hypertension in pregnancy is defined as, systolic blood pressure >= to 140, diastlolic blood pressure >= to 90 mm of Hg associated with proteinuria.

Hypertension in pregnancy is a challenge in modern obstetrics. Many people from different departments of medical practice have been involved in the research purposes.

Though the etiology of hypertensive disorder in pregnancy have been explained by many research workers over many years, the etiology remains unclear even today.

Many systems affected due to hypertension in pregnancy. In women with preeclampsia, renal function changes develop well before establishment of the symptoms and signs of pre eclampsia.

Many research works have been done to establish the correlation between hypocalciuria and development of pre eclampsia, so that it can be used as early predictor of pre eclampsia.

Several studies have been done in the past to find out the role of reduced excretion of calcium early detection of preeclampsia. In the early 1980 s they have shown that these

investigations may be used as a screening method in predicting hypertension in pregnanacy.

Since then, various trails have been trying to detect effectiveness of hypocalciuria in predicting pre eclampsia. Many other trials have failed to show the effectiveness of the low calcium excretion as a screening method.

So the need to establish the predictive values of this investigation and thus the efficacy as a screening test in predicting the high risk women. Multiple predictive tests have be put forth till date for prediction of pre eclampsia, but all of limited use for example,

ROLL OVER TEST

A hypertensive response induced by having women at 28 to 32 weeks of gestation assume supine position after lying laterally recumbent predicts gestational hypertension

ANGIOTENSIN SENSITIVITY TEST

A woman destined to get pre eclampsia will respond to less than 8ng/kg/min of n angiotensin infusion due to an alteration in vessel wall refractoriness,this test done between 26 to 30weeks.

PLATELET VOLUME

Thrombocytopenia and platelet dyfunction are the integral features of pre eclampsia. Increased destruction causes the platelet volume to increase because of relatively younger and therefore larger platelets entering the circulation. Ahmed et al found high platelets volumes to be a marker of impending pre eclampsia but with a substantive overlap with normotensive women.

SERUM FIBRONECTIN

Endothelial cell activation is the likely cause of elevated serumcellular fibronectin value in the population

with pre –eclampsia,in a study those levels rise within 12 weeks of gestation are high risk for developing pre eclampsia

UTERINE ARTERY DOPPLER

Uterine artery impedance between 18 to 26 weeks is being used as an early predictor of pre eclampsia.

ANTOTHROMBIN III LEVELS

URINARY KALLIKREIN EXCRETION

Ratio <170 between 16 to 20 weeks of pregnancy predicts pre eclampsia.

Though many number of predictive tests are available, none has been proved to be very sensitive and specific to predict pre eclampsia. Hence many randomized control trials are to be conducted to prove one test which is both sensitive

and specific to predict pre eclampsia, with good positive and negative predictive value.

AIMS & OBJECTIVES

AIM

To Asses the predictive value of calcium creatinine ratio in spot urine sample for early prediction of pre eclampsia

OBJECTIVES

To asses predictive value of calcium creatinine ratio

To asses maternal outcome

To assess the mode of delivery

To assess the fetal outcome

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Hypertensive disorders of pregnancy constitute the most common medical disorders encountered by obstetricians.

The incidence is 7% to 10 %,of which pre eclampsia/ eclampsia constitute 70% and chronic hypertension 30%. It remans the leading cause for maternal mortality and morbidity worldwide accounting for 15 % to 20%.

Pre eclampsia/eclampsia is a multi organ disorder unique to human pregnancy. Pritchard stated that the presence of chorionic villi in certain women incites vasospasm, hypertension and serious organ dysfunction, especially of placenta, kidneys, liver and sometimes brain.

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SERUM FIBRONECTIN

Endothelial cell activation is the likely cause of elevated serum cellular Fibronectin levels in high risk women. Study those levels rose within 12 weeks of pregnancy are intended to progress to develop pre eclampsia.

UTERINE ARTERY DOPPLER

Uterine artery impedence between 18 to 26 weeks has been used as an early screening test for women at risk of pre eclampsia.

ANTOTHROMBIN III LEVELS

URINARY KALLIKREIN EXCRETION

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Though many number of predictive tests are available, none has been proved to be very sensitive and specific to predict pre eclampsia. Hence many randomized control trials are to be conducted to prove one test which is both sensitive and specific to predict pre eclampsia

Prediction of pre eclampsia by using urinary CCR, a study conducted in queen Elizabeth hospital, woodvile, by Raniolo E et al, this was a prospective study, calcium creatinine ratio was estimated in 392 women, they concluded that calcium to creatinine ratio assessed in symptomatic

antenatal mothers at 20 to 30 weeks gestation was not a satisfactory predictive marker for development of pre eclampsia.

The major variation among different population, in calcium levels suggests that it cannot be used as a screening method.

Phuapradit W et al, conducted a study in the OBG Department, Mahidol University, Thialand, they assessed 190 primigravidas, at 28 to 32 weeks of pregnancy without any risk factors, were involved in the study .

Pre ecalmpsia was noted in 6.8% of samples, pateints with pre eclampsia did not demonstrate reduced excretion of calcium than normal population (2).

Study conducted by Kazerooni T et al in Shiraz University Shiraz, Iran. Study involved 200 women; they showed that CCR was appreciably less in pre eclampsia patients with a significant P value.

They concluded that, Calcium creatinine ratio can be used as mode of routine screening for early prediction of pre-eclampsia. (3)

Anai T, et al, conducted study in the Department of Obstetrics and Gynecology, Medical College of Oita. Hypocalciuria in women with preeclampsia.

To assess the significance of hypocalciuria in pregnant women, 24-hour urinary calcium excretion and the CCR (mg/g) in random urine samples were measured in the

following 4 groups: 3 mild preeclamptic patients, 5 severe preeclamptic patients, 4 patients with intrauterine growth retardation (IUGR), and 10 healthy pregnant women.

The mean 24-hour urinary calcium excretion in the 4 groups was 44.3 +/- 21.3 mg/day, 11.6 +/- 2.7 mg/day, 161.4 +/- 80.4 mg/day and 145.0 +/- 45.0 mg/day, respectively. Calcium excretion was significantly lower in the mild and severe preeclamptic patients than in the women with IUGR and the normal pregnant women.

There was also a significant difference between the value in the mild and severe preeclamptic patients. The mean calcium/creatinine ratio in random urine samples was 53 +/- 30 mg/g, 18 +/- 5.6 mg/g, 192 +/- 85 mg/g and 169 +/- 70 mg/g, respectively. Also, such significant as 24-hour urinary

calcium excretion were found in the mean calcium/creatinine ratio.

They concluded saying that determination the CCR in random urine samples is a reliable index of preeclampsia.(4)

Study conducted by Ozcan T et al in the Maternity Hospital, Turkey.

They conducted a study by testing the CCR and the calcium level in urine sample in 56 antenatal mothers, 44 among the 56 samples had normal CCR and hypertension developed in 8. The mean CCR was estimated the values to be significantly lower in the preeclamptic group compared with the normal group with significant p value.

A threshold value of CCR was 0.066 for the CCR were statistically analysed and had sensitivity of 75%, a specificity of 86%, and a positive and negative predictive value of 55%

and 95%, respectively. The results conclude that CCR can be used as screening tool for prediction of pre eclmapsia.

Saudan PJ et al conducted a study in Dept of Renal Medicine, University of New South Wales, Australia.

They wanted to prove the fact that Hypocalciuria has been associated with hypertensive disorder in pregnancy with or without proteinuria, but not with normal pregnancy.

They stressed up on the fact that reduced CCR has high sensitivity in detecting the pre eclampsia among high risk women. 81 antenatal mothers with established hypertension after 12 weeks of pregnancy were included in the study.

The CCR was determined in a sp urine sample at first visit. The Patients were observed and subsequently classified according to development of preeclampsia post natally.on follow up, patients who developed pre eclampsia had low

calcium excretion antenatally, compared to the population who remained normotensive. Results of statistical analyses revealed sensitivity 68% and a specificity of 70%.

The pathogenesis of renal involvement in pre eclampsia has been proved to occur well before the establishment of symptoms.

This test cannot be used as a sceerning test as the test lacks sensitivity, as a predictor of pre eclampsia

Kazerooni T published a study conducted in Iran,

The trail conducted to define the predictive value of CCR in prediction of pre eclampsia. The CCR ratio was determined in a urine sample of 102 normal antenatal mothers from 20-24 weeks of pregnancy. The women were observed and categorized according to occurrence of pre-eclampsia.

The CCR was compared, were correlated by prevalence pre eclampsia. 8 women developed pre-eclampsia and 94 were found to have normal blood pressure. The variables like age, time of enrollment to the study and time of delivery were compared between the two groups, and they did not show any association.

Mean urinary calcium concentration in normotensive and pre eclampsia women, were statistically significant, with hypoclaciuria in pre eclampsia women ,with significant P value.

They concluded that in pre eclamptic group calcium creatinine ratio was low compared to normotensive group. spot urinary CCR can be efficacious mode of assessment of high risk women .(7)

Calcium excretion in preeclampsia was assessed by Sanchez-Ramos L et al in the Dept of OBG, Florida Health Science Center, Florida.

They compared 24-hour urine data from 143 obstetric patients: 33 with preeclampsia, 58 normotensives, and 52 patients with gestational hypertension. The mean maternal age, race, and parity of these three groups did not differ significantly.

The preeclamptic patients had significant hypocalciuria compared to people who had normal blood pressure .The blood pressure and proteinuria were significantly increased in the preeclampsia group .using statistical analysis a urine calcium threshold of 12 mg/dL was chosen as cutoff for prediction of preeclampsia, with a sensitivity, specificity, of 85% and 91%, respectively.

The PPV -85 and NPV - 91%.They concluded that Urinary calcium levels below 12 mg/dL may help distinguish preeclampsia from other hypertensive disorders of pregnancy.(8)

Efficacy of CCR in spot urine and proteinuria as a screening tool for preeclampsia.

A study published by Rodriguez MH et al in American journal was conducted in Dept of OBG, Southern California School of Medicine, Los Angeles.

88 normotensive gravid women between 24 and 34 weeks of gestation underwent urine evaluation for the presence of microalbuminuria and urinary calcium excretion (calcium/creatinine ratio).

Preeclampsia subsequently developed in 83% of patients with a high level of microalbuminuria (greater than

or equal to 11 micrograms/ml) and a low CCR .Conversely, 94% of women who did not demonstrate high microalbuminuria and a low calcium/creatinine ratio remained normotensive at the time of delivery.

These results suggest that changes in renal function are present in gravid women who are otherwise free of symptoms in which preeclampsia will eventually develop.

They concluded the study saying that testing for microalbuminuria and a CCR can be used as assessment tool in early prediction of preeclampsia.(9)

Hypocalciuria as predictor of preeclampsia. Study done by Sanchez et al showed that,

Hypocalciuria is associated with pre eclampsia, whether the symptoms occur before or after the pathogenesis set in, needs to be established .

In this study urinary calcium excretion was measured in 103 primigravida at risk for developing preeclampsia less than 24 weeks of pregnancy. Multiple 24-hour urine samples were collected 24 weeks, 32 weeks, and 33 weeks to term. Post delivery, the values were evaluated for the development of hypertensive disorder.

Patients who developed preeclampsia had hypocalciuria (169 +/- 30 mg/24 hours) when compared to normal population (298 +/- 15 mg/24 hours) with P value less than .05, this levels were observed during pregnancy. Statistical analysis was done and PPV and NPV were obtained for calcium excretion levels of 195 mg/24 hours.

The difference in the incidence of preeclampsia between pregnant women with calcium excretion values at or below 195 mg/24 hours and those with values above that level was highly significant .with P value less than .0001.

These observations suggest that hypocalciuria may be related to the progression of hypertensive disorder during pregnancy.

(11) The CCR and PROTEINURIA in Predictors of Preeclampsia published by Sheela CN et al.

Study conducted in Dept of OBG St. John's Medical College & Hospital, Bangalore

Aim was to evaluate the urinary CCR and proteinuria as a marker for early prediction of preeclampsia. They Screened 200 asymptomatic women attending their clinic for pre eclampsia by doing CCR in spot urine and also microalbuminuria at 20 to 24 weeks of pregnancy.

They had taken the cutoff of 0.04 .The results were analysed and they concluded saying that there was significant association between low calcium excretion and development of pre eclampsia.

Statistical results of sensitivity, specificity, PPV and NPV of 69.2%, 98.2%, 85.7% and 95.8% respectively and p value was statistically very significant. It was found to be a good test for prediction of preeclampsia.

The study determined that pre eclampsia is associated with low calcium excretion at threshold for CCR at 0.04, so CCR in spot urine can be used as screening method in early pregnancy as a primary prevention for development of pre eclampsia.

Diagnostic efficacy of proteinuria and the CCR in the early prediction of hypertensive disorder in pregnancy, published in Spanish by, Martínez de Giordano D et al, study was conducted in Cátedra de Clínica Obstétrica Perinatología H.U.M.N., Córdoba.

They have evaluated the biochemical and clinical parameters for early detection of their alterations in pregnant women with late preeclampsia. Eighty nine patients between 24 and 32 gestation weeks were studied. Fifteen of them (18%) developed arterial hypertension (mean 141.5 +/- 3mmHg).

The perinatal results, gestational age at delivery, birth weight and Apgar score of the newborns were not significantly different among the groups that were evaluated. The microalbuminuria was analyzed through radioimmunoanalysis and reactive strips for the immunochemical semi quantitative determination.

They concluded the study with above results mentioning that no significant differences were found among the results of each evaluated method. The RIA showed greater sensibility, greater specificity and greater positive or

negative predictive value with respect to other methods, but the differences were not wide enough to consider it the method of choice.

In the group of patients (n = 15) who developed arterial hypertension, all the biochemical methods showed a normality higher than 80%. They concluded that none of these methods used alone is useful for the early prediction of the appearance of preeclampsia

MATERIALS AND METHODS

MATERIALS AND METHODS

The study was conducted in the dept of OBG, PSG Hospitals, and Coimbatore from July 2012 to May 2013.

STUDY DESIGN

Prospective study

STUDY POPULATION

The study group consisted of 200 samples, randomly selected from the pateints attending the antenatal clinic from gestational age 24 weeks to 34 weeks.

INCLUSION CRITERIA

Singleton pregnancy

Gestational age 24 to 34weeks

Multipara with no history of hypertension

EXCLUSION CRITERIA

Chronic hypertension

Renal disease

Multiple Pregnancy

Autoimmune diseases

Diabetes complicating pregnancy

Previous abruption

Previous IUGR

Previous history of PIH

METHODOLOGY


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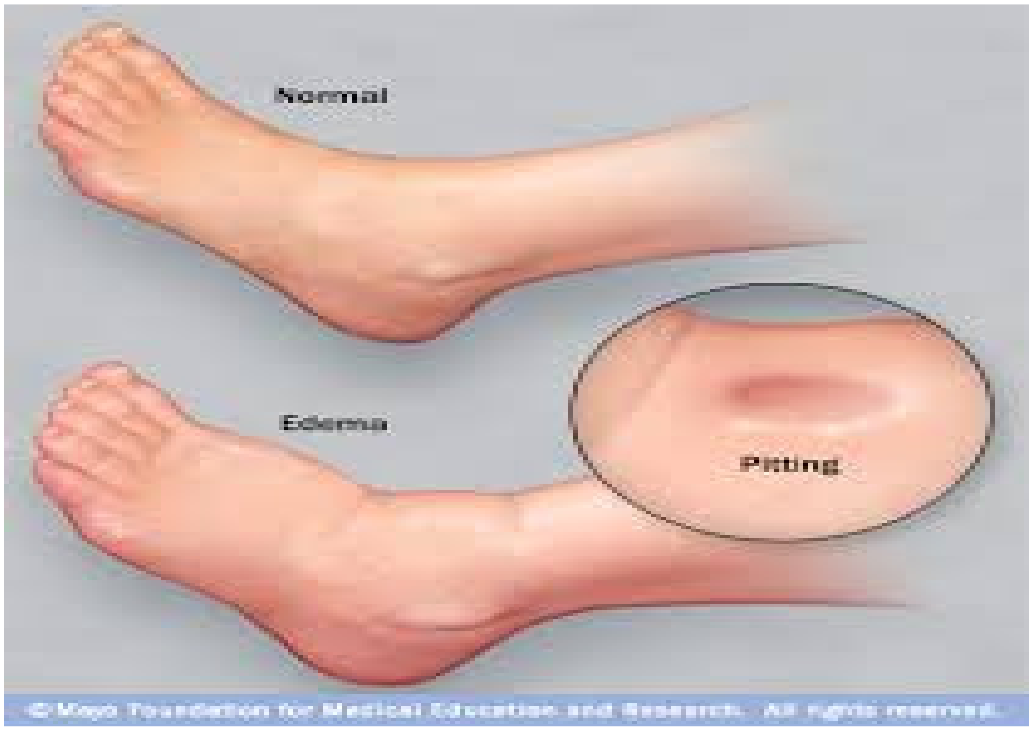
Normal
Edema
Pitting
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200 antenatal women who attended the PSG hospitals obstetrics and gynecology department outpatient department, from july 2012 to may 2013 at 24 to 34 weeks of gestation were enrolled in the study.

Informed consent was obtained from the patients for urinary CCR estimation.

Antenatal women with history of hypertension, diabetes and renal disease and women with the disorders mentioned in exclusion criteria were removed from the trail.

Women with a higher blood pressure of more than or equal to 140/90mm Hg were excluded from the study. All women were examined in detail and obtained history in detail about past and present illness. Anyone with the history suggestive of illness as mentioned in the exclusion criteria were not involved in the study.

Blood pressure (BP) was measured in the right arm sitting position. The urine sample was collected at the collection center and sent to bio chemistry laboratory for estimation of CCR.

The doctors and patients were blinded from the CCR values; they were observed and followed up regularly up to delivery.

Each and every patient involved in the trail was observed closely for signs and symptoms of pre eclampsia, like increased weight gain, reduced urine output, swelling of ankle, headache, epigastric pain, blurring of vision.

At delivery the mode of delivery and birth weight of the new born was noted to determine the secondary outcomes.
The data was collected at the end of the study and entered in the excel spread sheet and statistical analysis was done for

determing the sesnsitivity, specificity, PPV, NPV of CCR in determination of pre eclampsia.

GESTATIONAL HYPERTENTION

Defined as Blood pressure of more than or equal to 149/90 without protienuria

PREECLAMPSIA

Defined as blood pressure of more than or equal to 140/90 mmHg associated with protein excretion.

The women in the study were categorized bases on above definition as normotensive or hypertensive.

CCR values were determined and the levels less than or equal to <0.04+_0.04 were considered as low calcium excretion, I e positive,

Those with a ratio of >0.08 were considered as normal calcium excretion I e negative. The PPV, NPV, sensitivity, specificity of calcium to creatinine ratio is determined by

statistical analysis. Pearson correlation was established between normal group and the group who developed pre eclampsia with age, birth weight, and gestational age of development od pre eclmapsia

OUTCOME MEASURES

Development of pre eclampsia

Gestational age of development of pre eclampsia

Mode of delivery

Birth weight

PRO FORMA

NAME

AGE

SERIL NO

OP NUMBER

IP NUMBER

ADDRESS

UNIT

SOCIO ECONOMIC STATUS

MENSTRUAL HISTORY

OBSTETRIC HISTORY

GESTATIONAL AGE OFCOLLECTION

ANTENATAL COMPLICATION

PR

BLOOD PRESSURE AT BOOKING

EDEMA

ICTERUS

CVS

RS

PA

CALCIUM CREATININE RATIO

GESTATIONAL AGE OF COLLECTION

FOLLOW UP-

GESTATIONAL AGE OF DEVELOPMENT OF PRE ECLAMPSIA

COMPLICATION

MODE OF DELIVERY

BIRTH WEIGHT

PSG Institute of Medical Science and Research, Coimbatore

Institutional Human Ethics Committee

INFORMED CONSENT

I, Dr. SINDHU.D, MD., (OG) postgraduate from the department of Obstetrics and Gynecology of PSG Institute of Medical Science & Research (PSGIMS&R), am carrying out a study on the topic: To Asses the predictive value of calcium creatinine ratio in spot urine sample for early prediction of pre eclampsia.

Under the aegis of the Department of Obstetrics and Gynecology, PSGIMSR

The objectives of this study are:

To Asses the predictive value of calcium creatinine ratio in spot urine sample for early prediction of pre eclampsia.

Sample size: 200

Respondents are patients at 24 to 34 weeks of gestation, who attended the outpatient department. PSG hospitals coimbatore

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study.

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

RESULTS

Results

During the study period a total of 200 patients were included in the study.

BOX 1

No of postives and negatives

Test parameter	Test positive (n%)	Test negative (n%)	Total (n%)
CCR	**18 (9.0%)**	**182(91%)**	**200(100%)**

Among 200 samples 18 patients had abnormal CCR and 182 had normal values, i,e 18 were positives and 182 negatives CCR- Calcium Creatinine Ratio

BOX 2

The correlation of CCR with pre eclampsia

CCR	Pre-Eclampsia	Normotensive	Total
Test Positive	5 (2.5%) (True Positive)	13 (6.5%) (False Positive)	18 (9.0%)
Test Negative	2(1%) (False Negative)	180(90%) (True Negative)	182(91%)
Total	7(3.5%)	193(96.5%)	200(100%)

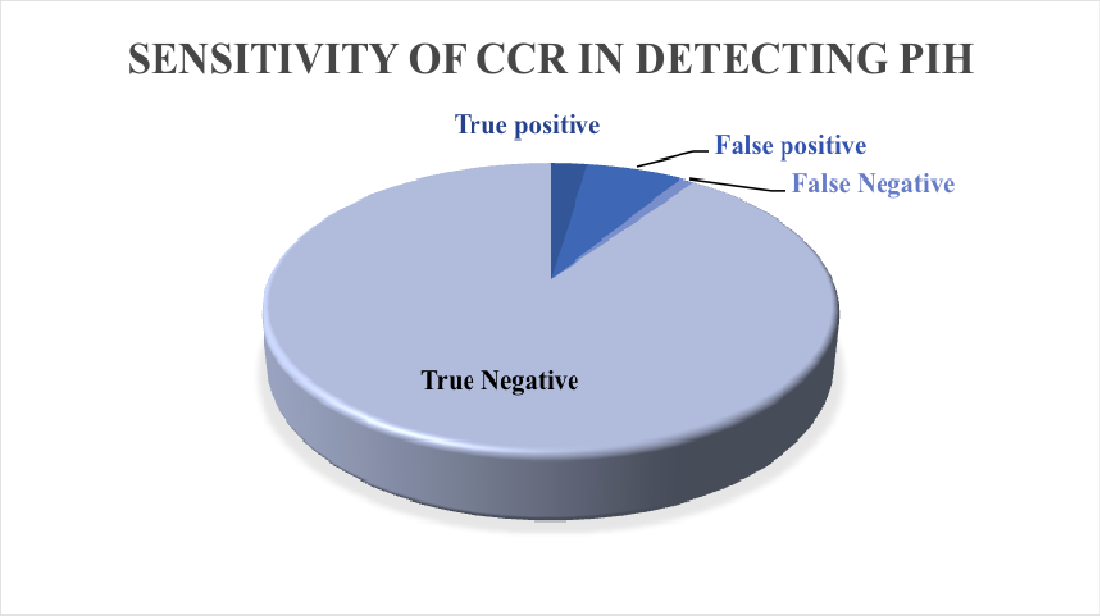


Fig 1

Among the 18 positive values,5 were true positives that is they developed pre eclampsia and 13 were false positive that is they failed to develop pre eclampsia, among 182 negative results ,2 were false negative meaning they developed pre eclampsia with normal CCR values and rest 180 were true negatives with normal CCR and normal blood pressure

BOX 3

Results of statistical analysis

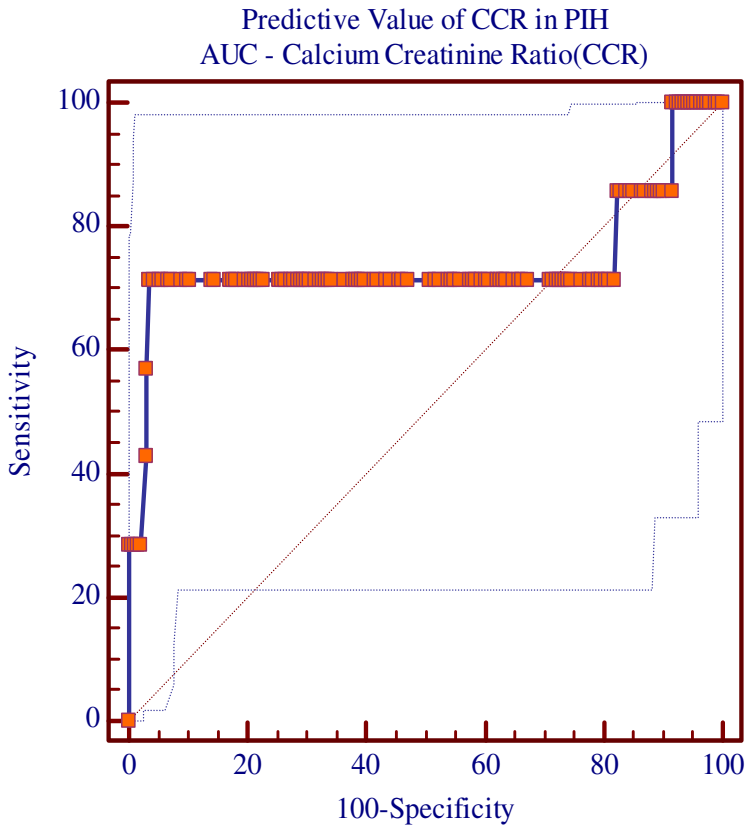
Test parameter	Criteria	Sensitivity	Specificity	PPV	NPV
CCR	≤0.04+_ 0.04	71.43	86.01	15.6	98.8

The sensitivity of CCR in prediction of pre eclampsia is 71% and specificity is 86%.

With very low PPV and good NPV of 98.8%

Area under curve of CCR

Fig 2



Test parameter	AUC	SE	95% CI
CCR	0.74	0.16	0.67-0.80

The Area under the Curve of CCR in predicting

Pre eclampsia is 0.74

Sensitivity is 71.43%

Specificity is 86.01%

The PPV is 15.6%

The NPV is 98.8%

BOX 4

Correlation of pre eclampsia and CCR with age, BW, GA at delivery

Pearson Correlation	CCR		Pre-Eclampsia	
	Correlation Coefficient	P Value	Correlation Coefficient	P Value
Age	0.100	0.160	0.075	0.293
BW	0.148	0.036	-0.029	0.682
GA at delivery	0.115	0.106	-0.065	0.362
CCR			-0.110	0.122
Pre-Eclampsia	-0.110	0.122		

CCR-Calcium Creatinine ratio

BW-Birth Weight

GA-Gestational Age

Normal CCR is found to have positive Pearson correlation with age, birth weight (BW) (statistically significant), implying that normal CCR samples had appropriate age, normal birth weight and term gestational age (GA) at delivery.

Whereas CCR has negative Pearson correlation with pre-eclampsia, suggesting that normal CCR had very low incidence of pre eclampsia.

BOX 5

Correlation of pre eclampsia with age, BW, GA of delivery and CCR

Parameters	Normotensive	PIH	P Value
Age	24.73	26.29	0.2926
BW	2.92	2.86	0.6825
GA at Delivery	38.75	38.29	0.3621
Calcium Creatinine Ratio	0.25	0.15	0.1221

CCR-Calcium Creatinine ratio

BW-Birth Weight

GA-Gestational Age

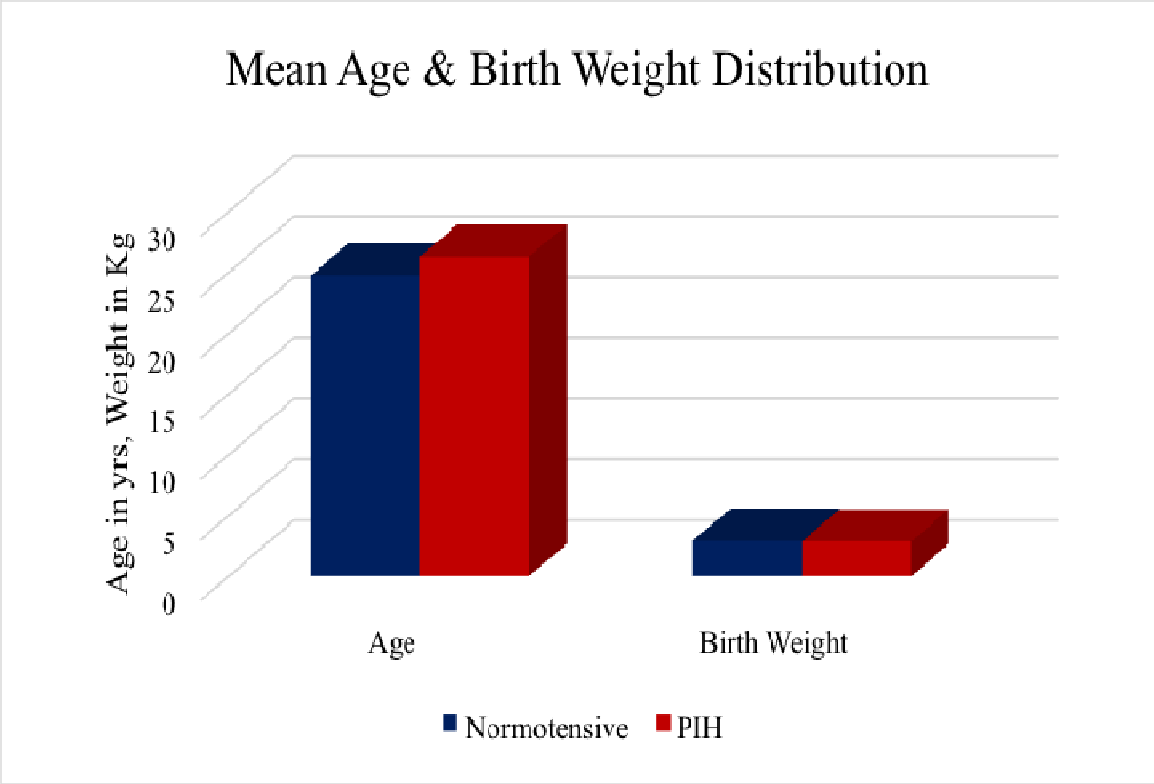


Fig 3

Diagnosis of Pre-Eclampsia has positive Pearson correlation with age, incidence of pre eclampsia is seen more common in younger age group.

Whereas Negative correlation with birth weight, gestational age and CCR,with P Value not significant

BOX 6

Correlation of CCR with age, BW, GA of delivery and CCR

Parameters	Normal CCR	Abnormal CCR	P Value
Age	24.73	25.28	0.566
BW	2.93	2.81	0.2338
GA at Delivery	38.74	38.67	0.8191
Calcium Creatinine Ratio	0.27	0.04	<0.01

CCR-Calcium Creatinine ratio

BW-Birth Weight

GA-Gestational Age

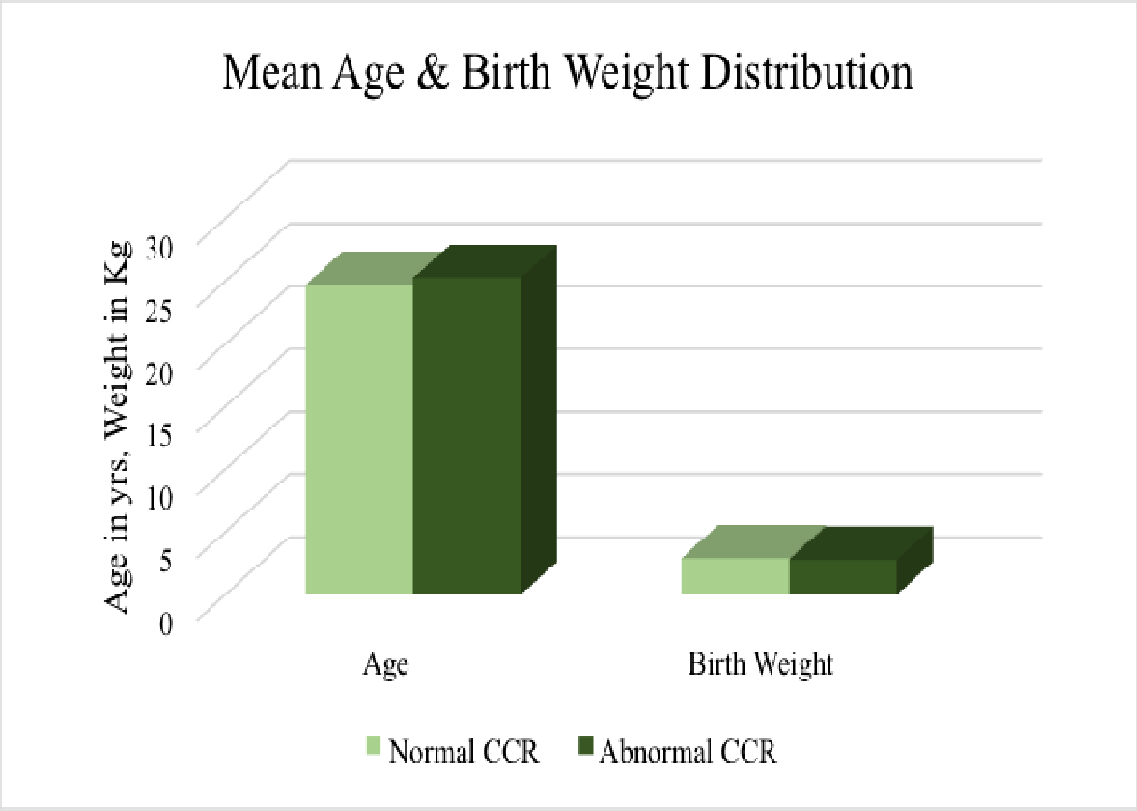


Fig 4

CCR is found to have positive Pearson correlation with age, birth weight (statistically significant) and gestational age, whereas CCR has negative Pearson correlation with pre-eclampsia.

BOX 7

Correlation of mode of delivery with CCR

Mode of Delivery	Normal CCR	%	Abnormal CCR	%
NVD	122	67.03	15	83.33
LSCS	59	32.42	3	16.67
IUD Term	1	0.55	0	0.00
Total	182		18	

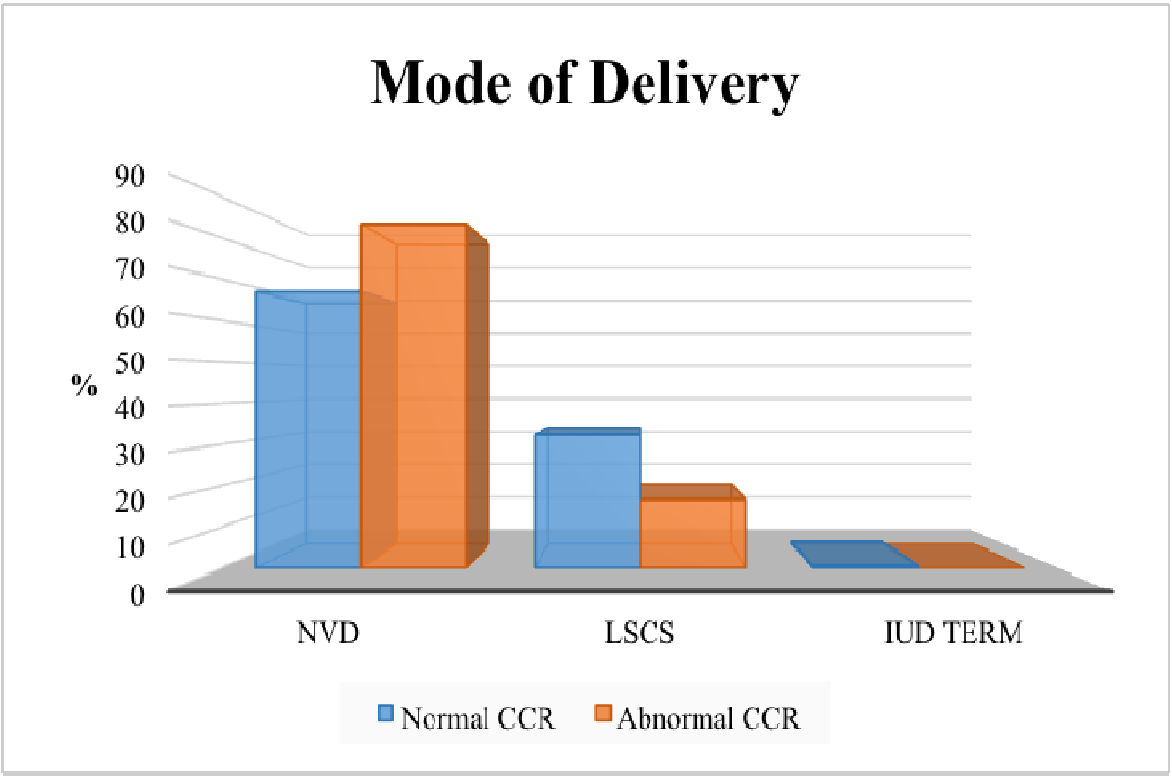


Fig 5

Mode of delivery had negative correlation with CCR, 83.3% of patients with abnormal CCR had normal delivery compared to normal CCR only 67% had normal delivery

BOX 8

Correlation of mode of delivery with pre eclampsia

Mode of Delivery	Normotensive	%	Pre eclampsia	%
NVD	132	68.39	5	71.43
LSCS	60	31.09	2	28.57
IUD Term	1	0.52	0	0.00
Total	193		7	

NVD - Normal Vaginal Delivery

LSCS – Lower Segment Caesarean

IUD –Intra Uterine Demise

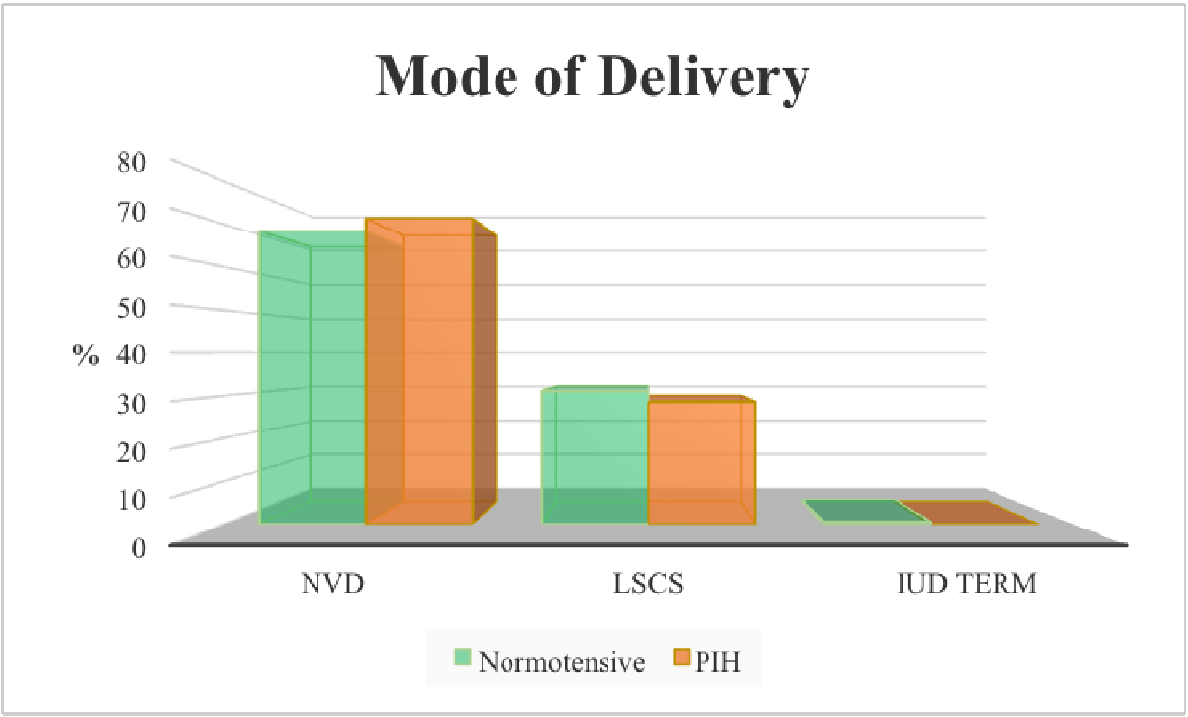


Fig 6

No significant correlation was established between mode of delivery and pre eclampsia.

DISCUSSION

DISCUSSION

In the above study comprising of 200 low risk anenatal mothers at 24-34 weeks of pregnancy were enrolled in the study. They all were assessed for development of pre eclampsia by determining the CCR in the urine sample.

They were categorized into pre eclampsia and normotensive depending on the low CCR less than or equal to 0.04 +_0.04 .Out of 200 samples, 18 calcium creatinine ratio was found to be abnormal, of which 5 developed pre eclampsia and rest 13 remained normotensive throughout pregnancy, and 2 samples with normal value developed pre eclampsia showing,

Sensitivity of 71%,

Specificity of 86%

NPV of 98.8%

PPV of 15.6%

Low calcium creatinine ratio has positive pearson correlation with the age, birth weight and gestational age of delivery, where as it has negative correlation with pre eclampsia.

Sheela et al , from St Jhons medical college conducted a study, Calcium creatinine and microalbuminuria in ratio in spot urine sample for prediction of pre eclampsia at 20 to 24 weeks of gestation they reported that, the sensitivity of 69.2%, specificity of 98.2%, PPV of 85.7% and NPV of 87% with statistically significant p value.

They concluded saying that a determination of CCR at less than or equal to 0.04, in a urine sample, in low risk women at 20-24 weeks of gestation is a better predictor

preeclampsia and can be recommended as a screening test for all pregnant women.

Where as in our study, we estimated only calcium creatinine ratio, and found to have sensitivity of 71%, specificity of 86% with a good NPV of 98.8% and PPV of 15.6%.

Concluding that CCR has got good NPV and better specificity but cannot be used as a routine screening method for prediction of preeclampsia, may be it can be used as more randomized trials with more sample size are needed for determining the efficacy of CCR in predicting pre eclampsia.

Ozcan conducted a trail where the efficacy of determining the hypocalciuria in urine sample for early prediction of pre eclampsia as early as in 1990 s and

concluded that low calcium excretion can be used as predictive marker of pre eclampsia.

Preeclampsia whereas the above study shows it can be used as a screening tool, in low risk group, but can be used in the high risk group for its high negative predictive value.

Saudan 6, had reported the sensitivity of Calcium creatinine ratio of only 68% and specificity of 70% with the threshold cut off value of 0.10,compared to the study stated above the threshold value is much lesser than the above value, which shows sensitivity of 71% and specificity of 86%,NPV of 98.8% and PPV of 15%.

Izumi had reported that the CCR had reduced value as a screening method of pre eclampsia, but screening was done in initial period of pregnancy, at less than or equal to 12

weeks, where as in the above study the gestational age is taken from 24 to 34 weeks, giving a wider range for prediction.

Kazeroomi et al and Kar et al established the efficacy of low calcium excretion in early prediction of pre eclampsia at less than or equal to 0.04 at 20-34weeks of pregnany and concluded saying that CCR can be used as a early marker of pre eclampsia.

Saudan PJ et al conducted a study in Dept of Renal Medicine, Australia.

They wanted to prove the fact that Hypocalciuria has been associated with hypertensive disorder in pregnancy with or without proteinuria, but not with normal pregnancy. They stressed up on the fact that low calcium excretion can be used

as a marker of imminent preeclampsia in women at high risk for developing preeclampsia. 81 women with established hypertension in second half of pregnancy were included in the study. The CCR was determined in a urine sample at first visit.

The Patients were observed and subsequently classified according to development of preeclampsia post natally.on follow up, patients who developed pre eclampsia had low calcium excretion antenatally, compared to the population who remained normotensive. Results of statistical analyses revealed sensitivity 68% and a specificity of 70%.

The pathogenesis of renal involvement in pre eclampsia has been proved to occur well before the establishment of symptoms .This test cannot be used as a sceerning test as the test lacks sensitivity for prediction of preeclampsia.(6)

Salako 10 has shown that urinary calcium excretion by determining CCR had a high sensitivity (88.9%) but a low PPV (22%), similar way as shown in the above study.

Estimation of CCR in a spot urine sample is a feasible test, easy to perform and hence has high patient acquiescence. It has a good NPV and hence substantiates the cost and it may be suitable to be used as a screening tool for prediction of preeclampsia.

It can therefore be suggested as a screening test for people who are high risk preeclampsia between 24-34 weeks of pregnancy.

Preeclampsia is a chief cause for maternal mortality and morbidity worldwide, especially in developing countries and there has been a many research works going on for a better predictor and there but prevention of pre eclampsia.

An accessibility of a good screening test would pledge and encourage more exploration work in the direction of primary prevention.

CONCLUSION

CONCLUSION

A single estimation of CCR at less than or equal to 0.04 +_0.04, in a spot urine sample, in asymptomatic pregnant women between 24-34 weeks of pregnancy, may be used as a early forecaster of pre eclampsia future development of preeclampsia in asymptomatic low risk women, but with high negative predictive value it can be used as screening tool for pre eclampsia in high risk group.

More randomized trials with the bigger sample size is needed for confirmation.

STATISTICAL ANALYSIS

STATISTICAL ANALYSIS

Data collected were entered in Excel Spread sheet and analyzed using STATA statistical software package release 11. We used the two-sided independent-samples t test to compare means across dichotomous variables; the one-way ANOVA test for comparison of means across multilevel variables. Simple calculations like Percentages, Proportions and Mean values were derived. A type I error of 0.05 was considered in all analyses. Using ROC - AUC, the sensitivity, specificity, positive and negative predictive value of the test is calculated.

BIBLIOGRAPHY

1) Med J Aust. 1993 Jan 18;158 (2):98-100 Prediction of pregnancy induced hypertention by means of the urinary calcium:creatinine ratio.

(2) Aust N Z J Obstet gynaecol.1993 Aug;33(3) :280-1.Urinary calcium to creatinine ratio in prediction of preeclampsia

(3) Int J Gynaecol Obstet. 2003 Mar;80(3):279-83.Calcium to creatinine ratio in a spot sample of urine for early prediction of pre-eclampsia.

(4) Nihon Sanka Fujinka Gakkai Zasshi. 1992 Jan;44(1):28-32. Hypocalciuria in women with preeclampsia.

(5) Am J Perinatol. 1995 Sep;12(5):349-51.

Urinary calcium to creatinine ratio for predicting preeclampsia.Ozcan T, Kaleli B, Ozeren M, Turan C, Zorlu G. Dr. Zekai Tahir Burak Maternity Hospital, Ankara, Turkey.

(6) Am J Hypertens. 1998 Jul;11(7):839-43.

Urinary calcium/creatinine ratio as a predictor of preeclampsia. Saudan PJ, Shaw L, Brown MA.

Department of Renal Medicine, St. George Hospital, University of New South Wales, Kogarah, Australia.

(7) Int J Gynaecol Obstet. 2003 Mar;80(3):279-83.

Calcium to creatinine ratio in a spot sample of urine for early prediction of pre-eclampsia.

Kazerooni T, Hamze-Nejadi S. Shiraz University of Medical Sciences, Shiraz, Iran.

(8) Obstet Gynecol. 1991 Apr;77(4):510-3.

Calcium excretion in preeclampsia. Sanchez-Ramos L, Sandroni S, Andres FJ, Kaunitz AM.

Department of Obstetrics and Gynecology, University of Florida Health Science Center, Jacksonville, Florida.

(9) Am J Obstet Gynecol. 1988 Dec;159(6):1452-5.

Calcium/creatinine ratio and microalbuminuria in the prediction of preeclampsia. Rodriguez MH et al

Department of Obstetrics and Gynecology, University of Southern California School of Medicine, Los Angeles.

(10) Obstet Gynecol. 1991 May;77(5):685-8.

Urinary calcium as an early marker for preeclampsia.

Sanchez-Ramos L, Jones DC, Cullen MT.

Department of Obstetrics and Gynecology, University of Florida Health Science Center, Jacksonville.

11) The Journal of Obstetrics and Gynecology of India January / February 2011 pg 72 – 76. Calcium-Creatinine Ratio and Microalbuminuria in Prediction of Preeclampsia

1Sheela CN et al Department of Obstetrics & Gynaecology, St. John's Medical College & Hospital, Bangalore – 560 034

(12) Rev Fac Cien Med Univ Nac Cordoba. 1993;51(2):15-20.

[Diagnostic value of microalbuminuria and the calcium/creatinine ratio in the early detection of preeclampsia]

(13) alhali A et al. Decreased fractional urinary calcium excretion and serum, 1,25- dihydroxyvitamin D and IGF-Ievels in preeclampsia. J Steroid Biochem Mol Biol 2007;103:803-6.

(14) Szmidt-Adjide V et al. Calciuria and preeclampsia: a case control study. Eur J Obstet Gynecol Reprod Biol 2006;125:193-8.

(15) Segovia BL, Vega IT, et al. Hypocalciuria during pregnancy as a risk factor of preeclampsia. Ginecol Obstet Mex 2004;72:570-4.

(16) Rodriguez MH, et al. Calcium/creatinine ratio and microalbuminuria in the prediction of preeclampsia. Am J Obstet Gynecol 1988;159:1452-5.

(17) Ozcan T, et al. Urinary calcium to creatinine ratio for predicting preeclampsia. Am J Perinatol 1995;12:349-51. Saudan PJ, Shaw L, Brown MA. Urinary calcium/creatinine ratio as a predictor of preeclampsia. Am J Hypertens 1998;11:839-43

(18) Izumi A, et al. Calcium-to- creatinine ratio in spot urine samples in early pregnancy and its relation to the development of preeclampsia. Metabolism 1997;46:107-8.

(19) Kazeroomi T, et al Calcium to creatinine ratio in a spot sample of urine for early prediction of pre- eclampsia. Int J Gynaecol Obstet 2003;80:279-83

(20) Kar J, et al. Role of urinary calcium creatinine ratio in prediction of pregnancy induced hypertension. J Obstet Gynaecol India 2002;52:39-42.

(21) Salako BL, et al. Microalbuminuria in pregnancy as a predictor of preeclampsia and eclampsia. West Afr J Med 2003;22:295-300.

(22) Shaaraway M, Salem ME et al The clinical value of microtransferrinuria and microalbuminuria in the prediction of pre-eclampsia. Clin Chem Lab Med 2001;39:29-34.

(23) Chhabra S, et al Prediction of pregnancy induced hypertension / preeclampsia by detecting micro albuminuria J Obstet Gynaecol India 2002;52:56- 60.

BIBLIOGRAPHY

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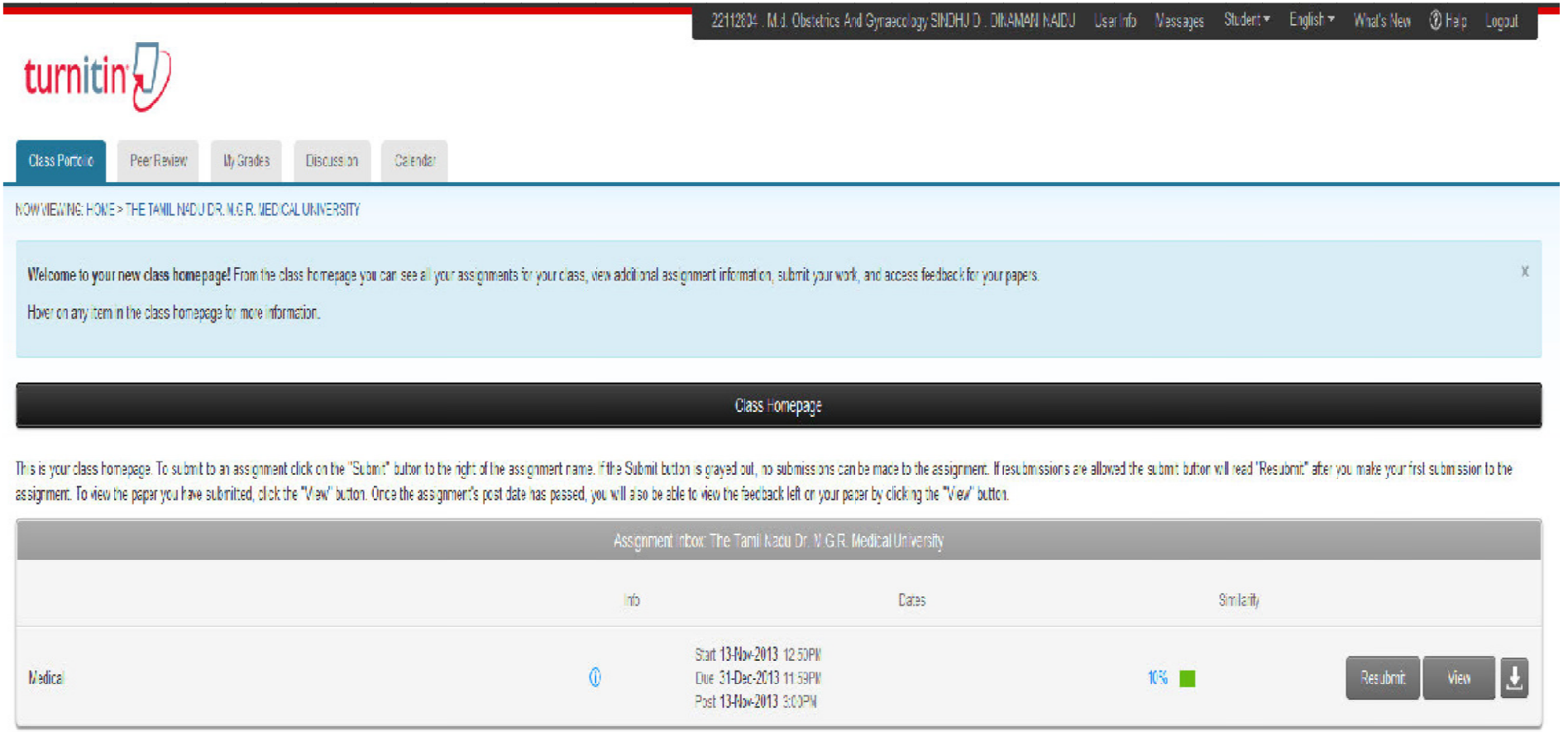
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Introduction

Hypertensive disorders during pregnancy constitute the most common medical disorders encountered by obstetricians. The incidence is 7% to 10 %,of which pre eclampsia and eclampsia constitute 70% and chronic hypertension 30%. It remains the leading cause for maternal mortality and morbidity world wide accounting for 15 % to 20%

Pre eclampsia/eclampsia is a multi organ disorder unique to human pregnancy. The typical renal lesions is glomeruloendotheliosis, which is the swelling of the glomerular capillary endothelial and mesangial cells. Involvement of renal system is well before the symptomatology of pre elampsia manifest. Pritchard stated that the presence of chorionic

PSG Institute of Medical Sciences & Research
Institutional Human Ethics Committee

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Phone : 91 422 - 2598822, 2570170, Fax : 91 422 - 2594400, Email : psgethics2005@yahoo.co.in

Proposal Number	:	**12/062**
Project Title	:	**Calcium to creatinine ratio in the spot urine sample for early prediction of preeclampsia**
Investigator(s)	:	**Dr D Sindhu**
Institution	:	**PSGIMS & R**
Name of the Guide(s)	:	**Dr K Kanchanamalai**
Institution	:	**PSGIMS & R**
Waiver of Consent	:	**No**
Review Type	:	**Exempt**
Date of the Meeting	:	**N/A**
Decision	:	**Approved**
Approval Date	:	**03.05.2012**
Validity of the Approval	:	**One year**

Approval for this study is given under the following terms and conditions:

1. Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.
2. PIs are required to send progress reports (in the form of an extended abstract with publications if any) to the IHEC every six months (and a month before expiry of approval date, if renewal of approval is being sought).
3. Request for renewal must be made at least a month ahead of the expiry of validity along with a copy of the progress report.

Dr Y S Sivan
Member - Secretary

SECRETARY
PSG IMS & R
COIMBATORE-641 004
INSTITUTIONAL HUMAN ETHICS COMMITTEE

S.No.	AGE	CCR	GA OF COLLECTION	GA OF PIH	GA OF DELIVERY	MODE	WEIGHT
1	24	0.204	26 WK		37 WK	LSCS	2
2	23	0.359	24 WK		39 WK + 6D	NVD	2.86
3	28	0.23	26 WK + 5 D		40 WK	NVD	2.92
4	24	0.204	25 W + 6 D		37 WK	LSCS	3.12
5	23	0.18	25 W + 6 D		39 WK	NVD	2.89
6	27	0.374	33 WK		38 WK	LSCS	2.98
7	23	0.44	26 W + 2 D		39WK + 5 D	NVD	3.02
8	18	0.242	25 WK + 3 D		39 W + 4 D	NVD	2.8
9	25	0.124	25WK + 6 D		39 WK + 6 D	LSCS	2.34
10	28	0.522	24WK + 3 D		39 WK + 2 D	LSCS	3.7
11	24	0.12	31 WKS		39 W+ 6 D	LSCS	3.96
12	36	0.11	24 WK + 6 D		38 WK + 4 D	LSCS	2.53
13	26	0.107	33 WKS		38 WKS	NVD	3.2
14	25	0.119	26 W + 2 D		37 WKS	NVD	2.7
15	27	0.18	24 WKS + 1 D		38 WKS	LSCS	2.23
16	23	0.15	24 WKS		40 WK	LSCS	3.4
17	28	0.159	26WK + 3 D		38 WKS	NVD	3.22
18	20	0.123	24 W + 1 D		39 WKS	NVD	2.96
19	18	0.035	28 WKS	38 WKS	39 WKS	NVD	2.94
20	22	0.166	33W + 1D		39 WK	NVD	2.98
21	21	0.169	29 WKS		40 WKS	LSCS	3.07
22	20	0.137	24WKS		35 WKS	NVD	1.98
23	27	0.408	24 WKS		39 WKS	NVD	2.73
24	20	0.12	25 W + 1 D		39 WKS	NVD	3.38
25	24	0.42	24 W + 5 D		38 WKS	LSCS	2.74
26	23	0.29	27 WKS		33 WKS + 5 D	NVD	2.14
27	25	0.07	25 W+ 6 D		36 WKS	LSCS	1.66
28	27	0.321	32 WKS		39 WKS	LSCS	3.1
29	25	0.307	30 WK + 1 D		37 WKS	NVD	2.35
30	24	0.15	25 WKS		37 WKS	NVD	2.8
31	27	0.116	31 WKS + 2 D		39 W + 4 D	NVD	2.87
32	26	0.3	29 WKS		40 WKS	NVD	2.97
33	21	0.246	26 WKS		39 WK + 3 D	LSCS	2.88
34	21	0.219	24WKS		39 W+ 6 D	NVD	3.25
35	22	0.118	24 W+ 1D		39 WKS	LSCS	2.49
36	23	0.394	24W + 5 D		38 WKS + 2 D	NVD	2.9
37	24	0.282	24 W + 4 D		38 WKS	LSCS	2.96
38	25	0.311	28W + 1 D		37 WKS	NVD	2.61
39	36	0.39	31 WKS + 3 D	32 WKS	38 WKS	LSCS	3.08
40	26	0.17	27 W+ 2 D		38 WKS	NVD	2.77
41	27	0.249	24 WKS		37 WKS	NVD	2.31
42	23	0.039	24 WKS		40 WK	NVD	3.14
43	26	0.161	29 WKS		39 W + 4 D	NVD	3
44	31	0.56	25 WK + 3 D		38 WK	NVD	2.9
45	26	0.144	29 WKS		40 WKS	NVD	3.12

46	28	0.22	28 WK + 4 D		40 W + 1D	NVD	2.48
47	27	0.62	27 WKS		39 WK +6D	LSCS	3.45
48	26	0.2	26 WKS		40 WK	LSCS	2.97
49	24	0.151	25 WK + 5 D		39 W + 4 D	LSCS	3.05
50	20	0.08	34 WKS		38 WKS +3 D	NVD	2.35
51	25	0.0236	32 WKS		38 WKS + 3 D	NVD	2.42
52	24	0.271	26 WKS + 3 D		40 WKS	NVD	3.64
53	34	0.09	24 WKS		40 WKS	NVD	3.57
54	30	0.205	28 WKS		39 W + 4 D	NVD	3.2
55	20	0.04	24 WKS + 6 D		39 WKS	NVD	2.96
56	24	0.11	24 WKS		38 WKS	NVD	3.11
57	30	0.42	24 WKS		39 WKS + 5 D	NVD	2.86
58	22	0.435	29 WKS		39 WKS + 3 D	NVD	2.8
59	23	0.066	29 WKS		40 WKS	NVD	2.56
60	20	0.259	26 WKS		37 WKS	NVD	2.76
61	25	0.19	27 WKS		38 WKS	LSCS	2.5
62	29	0.34	26 W + 2 D		38 WKS	LSCS	3
63	33	0.17	25 W + 3 D		40 WKS + 2 D	NVD	3.01
64	22	0.6	26 WKS + 2 D		39 WKS + 1 D	NVD	2.82
65	25	0.21	29 WKS		39 WK + 4 D	LSCS	3.13
66	23	0.25	28 WK + 6 D		37 WK + 6 D	NVD	2.9
67	27	0.44	24 WKS + 6 D		40 WKS	NVD	4.33
68	24	0.32	27 WKS + 4 D		36 WKS + 6 D	NVD	3.42
69	20	0.083	27 WKS + 2 D		38 WKS + 5 D	NVD	2.12
70	23	0.5	28 WKS + 4 D		40 WKS	NVD	3.1
71	26	0.16	25 WKS		37 WKS	NVD	2.45
72	21	0.3	28 WKS		38 WKS	LSCS	2.14
73	23	0.247	27 WKS		37WKS + 5 D	NVD	3.08
74	23	0.1	28 WKS		38 WKS + 3 D	NVD	2.42
75	27	0.154	28 WKS		38 WK + 4 D	NVD	2.9
76	21	0.095	28 WKS		39 WKS + 1 D	NVD	3.12
77	21	0.07	28 WKS		40 WKS	LSCS	2.9
78	26	0.17	28 WKS		40 WKS	NVD	3.3
79	24	0.25	27 WKS + 2 D		40 WKS	NVD	3.13
80	25	0.329	28 WKS		37 W + 2 D	NVD	2.21
81	26	0.12	28 WKS		39 WKS	NVD	3.33
82	23	0.192	25 WKS + 6 D		40 WKS	NVD	4.05
83	29	0.122	25 WKS + 1 D		39 WKS	LSCS	2.6
84	27	0.06	29 WKS		38 WKS	NVD	2.63
85	33	0.047	29 WKS		38 WKS	LSCS	3.3
86	34	0.011	27 WKS + 6 D		38 WKS	LSCS	2.3
87	20	0.007	25 W+ 6 D	38 WKS	39 WKS + 5 D	NVD	2.8
88	24	0.08	22 WKS		39 WKS + 5 D	NVD	3.31
89	26	0.03	26 WKS + 1 D	35 WKS + 6 D	39 WKS	LSCS	3.14
90	31	0.036	28 WKS + 3 D	30 WKS + 3 D	35WK + 1 D	NVD	2.25
91	25	0.511	29 WKS	36 WKS	37 WKS	NVD	2.9
92	21	0.09	28 WKS		38 WKS + 4 D	NVD	2.8
93	28	0.49	27 WKS		39 WK + 3 D	LSCS	3.8

94	27	0.161	24 WKS		39 W + 4 D	NVD	3.2
95	21	0.19	24 WKS + 5 D		38 WKS +3 D	NVD	3.1
96	22	0.176	26 WKS		40 WKS	NVD	2.8
97	22	0.156	24 WK + 5 D		40 WKS + 2 D	NVD	2.9
98	22	0.09	26 WKS		39 WKS + 6 D	LSCS	3
99	22	0.167	26 WKS + 5 D		39 WKS + 6 D	NVD	2.8
100	26	0.21	26 WKS		38 WK + 4 D	NVD	2.67
101	23	0.317	24 WKS		40 WKS + 2 D	LSCS	3.01
102	23	0.36	24 WKS + 4 D		40 WKS	NVD	3.01
103	27	0.264	27 WKS		37 WKS + 2 D	NVD	2.73
104	31	0.1	24 WKS + 5 D		40 WKS + 2 D	NVD	3.03
105	27	0.8	27 WKS		40 WKS + 2 D	NVD	3.1
106	27	0.109	26 W + 2 D		37 WKS + 5 D	LSCS	2.42
107	28	0.18	25 WKS		37 WKS	NVD	2.02
108	24	0.24	24 WKS		39 WKS + 6 D	LSCS	2.19
109	26	0.3	24 WKS		39 WKS + 4 D	LSCS	3.11
110	26	0.386	24 WKS		40 WKS	LSCS	3.22
111	29	0.1	24 WKS		38 WKS + 4 D	NVD	2.57
112	20	0.34	26 WKS + 1 D		39 WKS + 3 D	NVD	2.9
113	21	0.28	29 WKS		32 WKS	NVD	1.65
114	21	0.4	24 WKS		37 WKS + 3 D	NVD	2.95
115	26	0.5	25 WKS		39 WKS + 6 D	NVD	3.3
116	26	0.1	27 WKS		37 WKS + 3 D	NVD	2.5
117	18	0.24	25 WKS		39 W+ 6 D	NVD	2.9
118	22	0.33	24 WKS		40 WKS + 2 D	LSCS	3.9
119	26	0.03	25 WKS		37 WKS + 2 D	NVD	3.13
120	20	0.16	28 WKS		40 WKS	LSCS	3.75
121	27	0.2	30 WKS		38 WKS + 4 D	NVD	3.29
122	24	0.5	25 WKS		39 WKS + 4 D	LSCS	2.8
123	33	0.7	28 WKS		38 WKS	LSCS	3.15
124	26	0.36	24 WKS		38 WKS + 2 D	LSCS	2.75
125	18	0.16	26 WKS		37 WKS + 6 D	NVD	3.11
126	22	0.98	28 WKS		39 W + 4 D	NVD	2.8
127	24	0.168	26 WKS + 5 D		40 WKS	NVD	3.3
128	32	0.187	25 WKS		36 WKS + 4 D	NVD	2.42
129	27	0.241	29 WKS		40 WKS	LSCS	3.38
130	20	0.03	28 WKS		39 WKS + 3 D	NVD	3
131	21	0.121	25WKS		39 WKS + 1D	NVD	2.9
132	24	0.21	27 WKS		37 WKS + 6 D	NVD	2.3
133	26	0.01	24 WKS + 6 D		40 WKS	NVD	2.54
134	18	0.133	24 WKS		37 WKS + 6 D	NVD	2.87
135	26	0.2	26 WKS		38 WKS + 5 D	LSCS	2.8
136	24	0.33	24 WKS		39 WKS + 1 D	NVD	3.01
137	27	0.48	25 WKS		38 WKS	NVD	2.73
138	24	0.09	26 W + 2 D		39 WKS + 1 D	NVD	2.8
139	23	0.3	26 WKS		39 WKS + 5 D	LSCS	2.77
140	23	0.12	29 WKS		38 WKS + 4 D	NVD	3.34
141	28	0.25	28 WKS		37 WKS + 6 D	LSCS	2.73

142	26	0.29	30 WKS		38 WKS + 1 D	IUD TERM	2.6
143	19	0.24	28 WKS		37 WKS + 5 D	NVD	2.8
144	28	0.2	28 WKS		39 WKS + 5 D	LSCS	3.47
145	20	0.1	28 WKS		34 WKS + 6 D	NVD	1.98
146	23	0.08	24 WKS		39 WKS + 1D	NVD	2.98
147	32	0.2	28 WKS		37 WKS + 3 D	LSCS	3
148	23	0.9	24 WKS		39 WKS + 4 D	NVD	3.12
149	18	0.37	26 WKS		39 WKS	NVD	2.82
150	26	0.134	27 WKS		37 WKS + 3 D	NVD	2.5
151	21	O.286	29 WKS		38 WK	NVD	2.8
152	28	0.615	27 WKS		39 W+ 6 D	NVD	2.92
153	26	O.386	26 WKS		39 W + 4 D	LSCS	3.22
154	33	0.123	30 WKS		37 WKS + 4 D	LSCS	3.12
155	21	0.246	27 WKS		39 WKS	LSCS	2.88
156	31	0.67	26 WKS		40 WKS	NVD	2.95
157	23	0.28	29 WKS		40 WKS	NVD	3.25
158	19	0.197	29 WKS		40 WKS	NVD	3.5
159	18	0.16	26 WKS		37 WKS	NVD	3.11
160	20	0.489	26 WKS		40 WKS + 2 D	NVD	2.85
161	26	0.554	25 WKS		39WKS + 6 D	NVD	3.3
162	32	0.364	28 WKS		38 WKS + 2 D	LSCS	3.27
163	24	0.4	25 WKS		38 WKS +3 D	NVD	2.9
164	33	0.78	28 WKS + 2D		39 WKS	LSCS	3.15
165	29	0.403	28 WKS		38 WKS	LSCS	2.44
166	20	0.161	29 WKS		40 WKS	LSCS	3.71
167	32	0.155	27 WKS		38 WKS	LSCS	3.07
168	20	0.564	26 WKS		39 WKS + 3 D	NVD	2.9
169	24	0.19	26 WKS		40 WKS	NVD	3.4
170	23	0.8	29 WKS		38 WKS + 1 D	NVD	3.1
171	28	0.42	27 WKS		37 WKS	NVD	3.12
172	24	0.036	24 WKS		38 WKS + 4 D	NVD	2.8
173	23	0.07	30 WKS		38 WKS + 3 D	NVD	3
174	27	0.018	28 WKS		39 W+ 6 D	NVD	2.9
175	23	0.09	28 WKS		39 W + 4 D	LSCS	3.6
176	18	0.54	26 W + 2 D		40 W + 1D	NVD	3.1
177	25	0.3	26 W + 2 D		39WKS + 6 D	NVD	3.2
178	28	0.45	25 W+ 6 D		39 WKS + 6 D	LSCS	2.9
179	24	0.76	25WKS		39 WKS + 3 D	NVD	2.9
180	36	0.39	24 WK + 5 D		39 WKS + 3 D	NVD	3
181	26	0.23	25 WKS		39 WKS + 1D	NVD	3.11
182	25	0.33	26 WKS + 1 D		37 WKS + 6 D	NVD	2.86
183	27	0.3	27 WKS + 2 D		40 WKS	NVD	2.8
184	23	0.09	27 WKS		37 WKS + 6 D	NVD	2.56
185	28	0.06	24 WKS + 4 D		38 WKS + 5 D	NVD	2.76
186	20	0.2	25 W + 3 D		39 WKS + 1 D	LSCS	2.5
187	18	0.113	24 WK + 5 D		38 WKS	LSCS	3
188	22	0.14	26 W + 2 D		39 WKS + 1 D	NVD	3.01
189	21	0.2	27 WKS		39 WKS + 5 D	NVD	2.82

190	20	0.12	25 W + 3 D		38 WKS + 4 D	LSCS	3.13
191	27	0.308	25 WKS		37 WKS + 6 D	NVD	2.9
192	20	0.197	28 WKS		38 WKS + 1 D	NVD	4.33
193	29	0.111	26 WKS + 1 D		38 WK	LSCS	3.27
194	28	0.007	27 WKS	38+3D	39 W+ 6 D	NVD	2.9
195	25	0.3	27 WKS		34 WKS + 6 D	NVD	3.1
196	27	0.11	28 WKS		39 WKS + 1D	NVD	2.45
197	25	0.112	27 WKS + 4 D		37 WKS + 3 D	LSCS	2.14
198	24	0.282	26 WKS + 5 D		39 WKS + 4 D	NVD	3.11
199	26	0.34	26 W + 2 D		39 WKS	NVD	2.85
200	27	0.04	26 WKS		37 WKS + 3 D	NVD	3.3